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13. ABSTRACT ***(Maximum 200 Words)***

The purpose of this project is to evaluate the effect(s) of increasing fruit and vegetable intake on oxidative DNA damage and lipid peroxidation in a population of women at elevated risk for breast cancer. The rationale that underlies the work proposed is based on evidence that the occurrence of DNA mutations are essential steps in carcinogenesis and that these mutagenic events can result from oxidative stress, even in the absence of exogenous carcinogens. The effects of consuming a recipe-defined diet designed to provide three (control) or ten (intervention) servings of fruits and vegetables per day for a total of 8 weeks on measures of oxidative damage to DNA and lipids is being determined. During this reporting period, 160 individuals interested in the project were identified as eligible to participate. Of these candidate participants, 120 actually began the study and 92 have completed the study. Accrual to the study continues with the objective of completing accrual goals by April 2002. Evaluation of biological samples and dietary records is ongoing. However, since formal interim data evaluations are not a component of the analysis plan, no additional results are available.

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Introduction

The objective of this research project is to determine the effect(s) of increasing fruit and vegetable intake on oxidative DNA base damage and lipid peroxidation in a population of women at elevated risk for breast cancer. The rationale that underlies the work proposed is based on evidence that the occurrence of DNA mutations are essential steps in carcinogenesis and that these mutagenic events can result from oxidative stress, even in the absence of exogenous carcinogens. The effects of consuming a recipe-defined diet designed to provide three (control) or ten (intervention) servings of fruits and vegetables per day for a total of 8 weeks on measures of oxidative damage to DNA and lipids is being determined. Urine and blood components are being assessed for oxidative endpoints and plasma is being evaluated for biochemical markers of edible plant consumption.

Body

Approved Statement of Work

To test whether an increase in consumption of fruits and vegetables will decrease indicators of oxidative cellular damage in women at high risk for breast cancer occurrence or reoccurrence.

The activities required to complete the work statement were:

a. Initiate recruitment 2 months prior to initiation of a study group into the investigation.
b. Conduct the 8 week intervention in a total of 2 study groups (50 subjects, 25/group).
c. Perform laboratory analyses
d. Repeat steps a-c an additional three times (Years 1-3). We anticipate that recruitment will be completed during year three, and that laboratory and statistical analyses will continue throughout the project.
e. Summarize results and write reports and manuscripts (Years 1-3).

Project Implementation

Introduction As noted in the original application, this project was based on pilot work in which we studied the effects of a two-week recipe defined diet on oxidative markers. Upon commencement of work on this project, a multi-pronged plan of attack was implemented. Its elements included: 1) modification of the recipe-defined menus for use in an 8-week intervention study; 2) development and testing of intervention materials; and 3) further evaluation of the candidate oxidative markers. As reported in the First Annual Report, significant progress was made and recruitment was initiated. As outlined below, effort during the second year of the project has focused on conducting the intervention study.

Scheduling In order to maximize the likelihood of high dietary compliance, it was deemed very desirable to avoid major secular and denominational holidays during the course of the dietary intervention. Avoidance of July and August was also deemed desirable because of participant vacation schedules. During the calendar year, three blocks of time were identified as being most desirable and were targeted for recruitment efforts. Interventions were conducted during each of these time intervals during year 2 of the project.

Recruitment As might be anticipated, subject recruitment is a key aspect of this project and has required an exceeding amount of effort to be successful. One hundred sixty interested and eligible subjects were identified during this reporting period; however, we found that approximately 25% of individuals, making a verbal commitment to participate in a particular scheduled intervention, failed to actually enroll in the study. The most common reason given for deciding not to go forward with the expressed intent to participate was a work-related scheduling conflict that occurred during the 10-week recruitment period that preceded each intervention block.

Dropouts One hundred twenty individuals gave informed consent, enrolled in an intervention study, and gave specimens and dietary information. A total of 92 (76.7%) actually completed the study. Reasons for dropping out were categorized into three major categories: time constraints (e.g. work conflicts or insufficient time to prepare meals as required), 42.9%; unable to follow the diet (e.g. couldn't adjust to following a prescribed diet for an extended period of time, or didn't like the menus) 35.7%; and illness not related to the study (e.g. contracting flu or a severe cold). One individual who dropped was contacted for follow-up, but never returned phone calls or correspondence.

Adverse events No major or minor adverse events have been noted during the course of the project.

Sample evaluation Analyses of biological samples and dietary records are ongoing.

Statistical analyses If formal interim statistical analyses are performed, this would lower the p-value required to meet the criteria for statistical significance for reasons parallel to those associated with multiple comparisons. For this reason, it is deemed prudent to await the collection of all data and then subject the entire data set to formal statistical analyses.

Key Research Accomplishments

- A total of 160 interested and eligible participants were identified during year 2 of the grant and three intervention cycles were conducted. Of the 160 candidate participants who indicated their verbal intention to participate, 120 subjects actually gave informed consent and biological specimens. Of these individuals, 92 completed the intervention.
- Based on information gleaned from the first three intervention cycles, efforts have been directed to intensifying recruitment activity. It is anticipated that accrual goals will be completed by April 2002.

Reportable Outcomes (cumulative)

- Cookbooks were developed and tested .
- Supporting intervention materials were developed and tested.
- An alternative method of analysis of a urinary product of DNA oxidation was identified.
- Assessment of serum protein oxidation was shown to be feasible.

Conclusions During this reporting period 92 subjects completed the dietary intervention. It is anticipated that accrual goals will be completed by April 2002.

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